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Chronic Inflammatory Demyelinating Polyneuropathy in a Patient with Charcot-MARIE-Tooth (CMT) Disease Type 1A: Case Report

ABSTRACT

We report a patient with chronic inflammatory demyelinating polyneuropathy (CIDP) developed against hereditary motor-sensory polyneuropathy (Charcot-Marie-Tooth disease type 1A). It is shown that the presence of chronic persistent herpes infection, stratifying on the mutation in the gene PMP22 (peripheral myelin protein), may lead to the development of autoimmune process, manifested demyelinating lesions of the peripheral nerves of the limbs and cranial nerves. CIDP – an autoimmune disease characterized by lesions of the myelin sheath of peripheral nerves, it accounts for about 20-50% of undiagnosed polyneuropathy. The literature discusses the contribution of viruses of the family Herpes Viridae to the development of CIDP. Charcot-Marie-Tooth disease (CMT) – a large group of hereditary diseases of the nervous system characterized by chronic progressive weakness and atrophy of distal limb muscles, reduced tendon reflexes, foot deformities and hands, changes in gait and sensory impairments.

Keywords: Chronic inflammatory demyelinating polyneuropathy (CIDP), Charcot-Marie-Tooth (CMT) disease, comorbidity, case report.

INTRODUCTION

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired immune-mediated disease characterized by lesions of the myelin sheath of peripheral nerve fibers [5, 11]. CIDP difference from Guillain-Barre syndrome is a relatively slow progression of symptoms for more than 8 weeks [15], in children - up to 4 weeks [3, 6].

CIDP represents approximately 20-50% of initially undiagnosed neuropathies [10] and is the most common autoimmune demyelinating neuropathy. The prevalence of CIDP is 1,2-7,7 cases per 100,000 individuals [5].

Clinical features of CIDP are: 1) progressive symmetrical or asymmetrical polyradiculoneuropathy; 2) relapsing or progressive course (> 2 month); 3) proximal weakness usually prominent; 4) large filber sensory loss in the distal limb (vibration and join positive sense); 5) generalized hyporeflexia or areflexia [10, 11].

Clinical forms of CIDP include multifocal acquired demyelinating sensory and motor neuropathy (the Lewis-Sumner syndrome), sensory-predominant CIDP, distal acquired demyelinating symmetric neuropathy, and CIDP with a lesion of central nervous system [6, 11, 12]. Magnetic resonance imaging (MRI) of the brain has revealed demyelinating lesions in the central nervous system in some patients with CIDP, despite the rarity of cerebral or cerebellar symptoms [8, 11, 17, 18].

CIDP may be also associated with concurrent disease, such as infection with the human immunodeficiency virus or hepatitis C, Sjogran's syndrome, melanoma, lymphoma et al. Significant contribution to the development of CIDP make viruses of the family Herpes Viridae [2, 13]. Occasionally, CIDP may develop on a setting pf another polyneuropathy, even one with a hereditary basis, such as Charcot-Marie-Tooth [11].

Charcot-Marie-Tooth disease (CMT) is a large group of hereditary diseases of the nervous system characterized by progressive muscle weakness and atrophy of distal extremities, hyporeflexia, and deformation of foots and hands, changes in gait and sensory impairment [1]. Prevalence is approximate to 1:2500 [19].

A common classification uses as main criteria the inheritance patterns and molecular genetics: 1) CMT1, characterized by abnormal myelin, with an autosomal dominant mode of inheritance, is the most frequently (about 50% from all cases); 2) CMT2, having the main feature axonopathy, also an autosomal dominant form, is on the second place (approximately 20-40%); 3) Intermediate form, an autosomal dominant combination of myelinopathy and axonopathy in individual is rare; 4) CMT4 is a rare group of progressive motor and sensory axonal and demyelinating neuropathies; 5) X-linked CMT is characterized by a moderate to severe motor and sensory neuropathy in affected males and usually mild to no symptoms in carrier female and is responsible for approximately 10-20% from cases [1, 19].

CMT1 – as well as the others subtypes of CMT can be further subdivided primarily on molecular genetic findings. Each of these subtypes is identified based on detection of a mutation in the causative gene: PMP22 – Peripheral myelin protein 22 (subtypes 1A and 1E), MPZ – Myelin P0 protein (subtype 1B), EGR2 – Early growth response protein 2 (subtype 1D), and NEFL – Neurofilament light polypeptide (subtype 1F) [1, 19]. The CMT1 subtypes are often clinically indistinguishable. The most common form is CMT 1A type with an autosomal dominant mode of inheritance, the cause of which is a mutation in the gene PMP22 [21].

Currently, there is evidence according to which there may be cases of CIDP in patients with CMT [7, 9, 14]. M. Watanabe et al. (2002) described the development of inflammatory neuropathy in patients with type CMT 1B, which was positive dynamics in the neurological symptoms in response to corticosteroid therapy [22]. In the same year, Gabriel C. et al. based on clinical, immunological and histological studies in 12 patients with CMT type 1A found that at step progression of the disease is likely to have the inflammatory component, layered on the genetic background [20]

In this article, we report own clinical observation of 19-year-old female patient with Charcot-Marie-Tooth disease type 1A, which has developed a pattern of chronic inflammatory demyelinating polyneuropathy with remitting course.

CASE REPORT

The patient is a 19-year-old girl. She admitted to the neurological department of the Republican Hospital №2 – The Center emergency medical care (Yakutsk city) in January 2015 with complaints of unsteadiness of gait, lack of movement in the facial muscles on both sides, constant drooling, speech problem, choke when taking the liquid and solid foods, decreased vision in both eyes, expressed general weakness, daytime sleepiness, fatigue, intermittent dizziness turning the head, constipation.

Medical history: The first neurological symptoms appeared after acute viral infection in February and March 2010 in the form of repeated transient sensory disturbances on the face (feeling cold), numbness of the tongue and partial violation of articulation. In April, the patient vaccinated against influenza H1N1. In May, there were severe infectious symptoms: fever up to 39 ° C, general weakness, loss of appetite, nausea, diparesis of mimic muscles, left-sided facial hemianesthesia, dysarthria, dysphagia, vertigo. A patient was hospitalized in the pediatric center of the Republican Hospital №1 with stem encephalitis. Detected in cerebrospinal fluid protein-cell dissociation (protein level of 1.2 g / l in normal cell count). Linked immunosorbent assay was positive for cytomegalovirus, mycoplasma and chlamydia. Electroneuromyography (ENMG) significant impairment of axonal-demyelinating by type, more pronounced on the facial nerve. MRI of the brain was without pathology. Given the family history of CMT maternally (sick sister's son and brother of the mother) a patient was examined by a clinical geneticist, subsequent DNA diagnosis has identified gene duplications peripheral myelin protein (PMP22) on chromosome 17r11.2-12. A patient was diagnosed CMT type 1A. The department received a course of antiviral, immunomodulatory therapy. The girl was discharged with the positive dynamics: devolution of

infectious symptoms, decrease bulbar disorders, the emergence of movements in the facial muscles. A patient examined at the Children's Clinical Hospital in Moscow, where the diagnosis CMT type 1A was confirmed.

Since October 2014, a patient increased weakness, decreased appetite, dizziness, an expression of a systemic nature, increased weakness in the facial muscles, increased salivation, choking when receiving the liquid and solid food. In January 2015, she admitted to the neurological department.

Patient was born on the fourth child in the family; the mother pregnancy was uneventful, natural childbirth. Physical and mental development by age. Menstruation from 14 years, painless, regular. Currently studying for a 3-year university, with learning to cope.

State of medium severity. Skin is pale and clean. Visible mucous pale pink and clean. No peripheral edema. Palpable enlarged, not welded submandibular lymph nodes, painless. Nasal breathing freely, breathing in the lungs vesicular, taken over all the fields, no wheezing. Heart tones are muffled, rhythmic. Hypotension to 90/60 mm Hg, tachycardia up to 108 per minute. Language moist, clean. Abdominal palpation soft, painless. Liver and spleen were not palpable. Symptom effleurage negative on both sides. Urination free, painless enough. Tendency to constipation.

Patient oriented in space, time and self. Several not critical, intelligence corresponds to the age and education. Moderately elevated levels of situational anxiety. The general background mood somewhat depressed. On the part of the cranial nerves: convergent strabismus easy due to OU, diplegia of mimic muscles, horizontal nystagmus, bulbar syndrome (dysphagia, dysphonia, dysarthria, decreased gag reflex, drooping soft palate, tongue muscle atrophy with fasciculations). Tetraparesis with strength in distal muscle groups of the upper and lower limbs to 4 points, proximal muscle strength 5 points. Low muscle tone, severe diffuse muscle wasting, muscle wasting interdigital spaces. Reflexes from the hands are normal, uniform; knee reflexes uniformly reduced; Achilles reflexes are reduced, uniform. High arch, foot deformity by type Fridreykh. Sensitive no violations. Coordination tests performs with mild ataxia. Sensory ataxia. Pelvic function controls.

Patient went follow-up investigation.

ELISA HIV is negative.

ELISA virus family Herpes viridae: moderate increase in titers of immunoglobulin G and M to cytomegalovirus and herpes simplex virus type 2. In the immune status had elevated levels of immunoglobulin G and M (156 g / L and 13.5 g / l respectively).

According to the visual evoked potentials to reverse chess pattern revealed no pathology.

Stimulation ENMG facial nerve showed signs of axonal-demyelinating type conduction abnormalities on both sides.

MRI of the brain revealed symmetrical affected area (cytotoxic edema) legs of the cerebellum on both sides of the spread in both hemispheres of the cerebellum (the size of the right 4,3x1,6 cm., Left - 3,4x1,6 cm.) With a weak accumulation of contrast agent with intravenous contrast enhancement. Revealed the accumulation of contrast material in the course of the temporal part of the facial nerve on both sides and small areas of glial changes in the posterior portions of the bridge. Conclusion: reliably judge the nature of the observed changes is not possible, probably holds the active demyelinating process.

On the basis of complaints, history of the disease, the characteristic clinical manifestations, paraclinical data and immunological research, clinical diagnosis was established:

The main diseases: chronic inflammatory demyelinating polyneuropathy, mainly affecting cranial and bulbar group of nerves at the stage of exacerbation. Diplegia of mimic muscles. Bulbar syndrome. Easy distal tetraparesis. Sensory ataxia. Group risk of aspiration.

Background diseases: Charcot-Marie-Tooth disease type 1A of autosomal dominant inheritance, moderately progressive course.

Chronic mixed-herpes-virus infections: cytomegalovirus infection in the stage of replicative activity of HSV-1 infection. Secondary immunodeficiency in violation of the anti-viral infectious response.

The department patient received 3 sessions of plasmapheresis, pulse-hormone therapy, intravenous immunoglobulin course (IVIG), vitamin therapy. At discharge condition with some improvement in the form of reducing the overall weakness, improvement of appetite.

CONCLUSION

Stepwise progression of neurological deficits in patients with hereditary forms of neuropathy requires a more careful examination of their stratification to identify inflammatory demyelinating component. Chronic herpes infection starts a secondary dis- immune disorder of the peripheral nervous system by type of CIDP in the presence of predisposition to chronicity and recurrence of herpes virus infection, particularly in patients with a genetic defect of the protein

RMR22. CIDP, unlike CMT, refers to a group of potentially curable diseases and timely diagnosis; treatment significantly may affect the quality of life of patients. Layering on CIDP in CMT weights clinical course of two competing diseases.

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